PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 41543PCT0302	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US04/26035	International filing date *(day/month/year)* 11 August 2004 (11.08.2004)	Priority date *(day/month/year)* 11 August 2003 (11.08.2003)
International Patent Classification (IPC) or national classification and IPC IPC(7): C07H 21/04; C12Q 1/68 and US Cl.: 435/6; 536/23.1		
Applicant LOVELACE RESPIRATORY RESEARCH INSTITUTE		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10 June 2005 (10.06.2005)	02 August 2005 (02.08.2005)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Jeanine Enewold Goldberg Telephone No. (571) 272-1600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US04/26035

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed.

☒ the description:
pages 1-37 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages NONE, as originally filed
pages 38 and 39, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-3, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. 18-21

☒ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US04/26035

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-19	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 1-19	YES
	Claims NONE	NO
Industrial Applicability (IA)	Claims 1-19	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-19 meet the criteria set out in PCT Article 33(2) and 93), because the prior art does not teach or fairly suggest an association between an exon 6 codon 279 Gln/Arg SNP within MMP-9 as associated with COPD (chronic obstructive pulmonary disorder). The prior art teaches MMP-9 polymorphisms which include the codon 279 Gln/Arg mutation (see Zhang - WO 99/57315, 11 November 1999). The prior art also analyzed the 279 Gln/Arg SNP with coronary artery disease and cardiovascular disease. However, neither of these studies suggests COPD.

Claims 1-19 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry.

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claim 19 is objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: Claim 19 depends on claim 22 which is no longer pending. The cancellation of original claims 18-21 appear to use this artifact numbering.

CLAIMS

What is claimed is:

1. A method for determining the susceptibility of an individual to a chronic obstructive pulmonary disorder (COPD), comprising the step of determining the presence of an exon 6 codon 279 Gln/Arg single nucleotide polymorphism within the matrix metalloproteinase-9 (MMP-9) locus in a biological sample obtained from the individual, wherein the 279 arginine polymorphism indicates susceptibility to chronic obstructive pulmonary disorder.

2. The method of claim 1, further comprising use of an isolated nucleic acid molecule to detect the codon 279 Gln/Arg single nucleotide polymorphism.

3. The method of claim 2, wherein the isolated nucleic acid molecule is DNA, cDNA or mRNA.

4. The method of claim 2, wherein the isolated nucleic acid molecule is a single-stranded or double-stranded nucleic acid molecule.

5. The method of claim 2, wherein the isolated nucleic acid molecule is a probe which hybridizes under stringent conditions to a particular allele of the polymorphism.

6. The method of claim 5, wherein the probe comprises the sequence 5'-CTCTACACCCGGGACGGCAATG (SEQ ID NO:1).

7. The method of claim 5, wherein the probe comprises the sequence 5'-ACTCTACACCCAGGACGGCAATGC (SEQ ID NO:2).

8. The method of claim 2, further comprising use of a nucleotide primer which amplifies a particular allele of the polymorphism.

9. The method of claim 8, wherein the nucleotide primer comprises a 5'-TCTCCCCCTTTCCCACATC (SEQ ID NO:3) sense primer or a 5'-TGTGCTGTCTCCGCCTTCT (SEQ ID NO:4) antisense primer.

10. The method of claim 1, wherein determining the presence of an exon 6 codon 279 Gln/Arg single nucleotide polymorphism within the MMP-9 locus comprises testing expressed protein for the presence or absence of arginine in the 279 position.

11. A method of determining the efficacy of a substance to inhibit the 279Arg MMP-9 enzyme for use as a therapeutic or preventive agent for COPD, the method comprising the steps of:

providing the 279Arg MMP-9 enzyme; and

testing the substance for inhibition of the 279Arg MMP-9 enzyme.

12. The method of claim 11, wherein providing the 279Arg MMP-9 enzyme comprises inserting a gene expressing the 279Arg MMP-9 enzyme into a cell line.

13. The method of claim 12, wherein the gene expressing the 279Arg MMP-9 enzyme is SEQ ID NO:11 where 841 n is guanine (G).

14. The method of claim 11, further comprising the steps of:

providing the 279Gln MMP-9 enzyme;

testing the substance for inhibition of the 279Gln MMP-9 enzyme; and

comparing the results obtained for inhibition of the 279Arg MMP-9 enzyme with results obtained for inhibition of the 279Gln MMP-9 enzyme.

15. The method of claim 11, wherein the 279Arg MMP-9 enzyme is purified enzyme.

16. The method of claim 14, wherein the 279Arg MMP-9 enzyme and the 279Gln MMP-9 enzyme are each purified enzyme.

17. The method of claim 14, wherein the gene expressing the 279Gln MMP-9 enzyme is SEQ ID NO:11 where 841 n is adenine (A).

18. A method of treating a patient with COPD or at risk for developing COPD, comprising the steps of:

determining the presence of an exon 6 codon 279 Gln/Arg single nucleotide polymorphism within the MMP-9 locus in a biological sample obtained from the patient;

administering an MMP-9 inhibitor to the patient with a 279 arginine polymorphism.

19. The method of claim 22, wherein the MMP-9 inhibitor is a selective 279Arg MMP-9 enzyme inhibitor.